

REMARKS

Introductory Comments

Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are pending. Claims 39, 42, 44, 47, 48, 50, and 69-79 have been canceled. Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are rejected.

The Examiner has rejected claims 38 and 65-68 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner has rejected claims 38, 40, 41, 43, 45, 46, 49, and 65-68 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner has rejected claims 38, 40, 41, 43, 45, 49, and 65-68 under 35 U.S.C. §112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

These rejections are believed to be overcome in part by the amendments and are otherwise traversed for reasons discussed below.

Overview of the Amendments

Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 have been amended without prejudice or disclaimer. Amendment of these claims is not intended to be an acquiescence in the Office's assessment of those claims in the 1 February 2001 Communication, and applicants expressly reserve the right to bring the subject matter of the original claims again in a subsequent, related application.

Basis for the amendments to claim 38 can be found throughout the specification, for example, at least at the following locations: page 17, lines 25-30; and pages 61-69.

Basis for the amendments to the rest of the claims can be found throughout the specification. Primarily the amendments to the dependent claims (i.e., all claims but claim 38) are made to provide appropriate antecedent basis for terms used therein.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

Addressing the Examiner's Rejections

1. Rejection of Claims 38 and 65-68 under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 38 and 65-68 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants disagree with the Examiner's assessment of the claims. The claims and teachings of the specification, taken in combination with methods of generating and screening transgenic animals known in the art, reasonably convey to one of ordinary skill in the art the scope and content of the present invention. However, in order to facilitate prosecution of this application, applicants have limited the claims to transgenic mice. Numerous mouse control elements (e.g., promoters) useful in the practice of the present invention are described in the specification and, in particular, numerous mouse stress-inducible gene derived control elements are described (see, for example, specification pages 35-41). Methods of generating the reporter constructs of the present invention are described (see, for example, specification pages 58-59). Methods of generating and screening transgenic mice are known in the art and further some specific methods for generating transgenic animals are described in the specification (see, for example, specification pages 61-69). Further, the evaluation of expression mediated by the selected control elements of the present invention is also described (see, for example, specification pages 59-61).

In view of the above amendments and arguments applicants submit that the claims comply with the requirements of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph, is respectfully requested.

2. Rejection of Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 38, 40, 41, 43, 45, 46, 49, and 65-68 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner asserts that in order to practice the claims of the present invention undue experimentation would be required. Repeatedly the Examiner asserts that the specification is not enabling for producing “any and all transgenic animals comprising more than one expression construct because the specification does not provide sufficient guidance, evidence, and working examples to make all the transgenic animals and because the art of making transgenic animals is highly unpredictable. (e.g., Office action, page 5, last paragraph). The Examiner lists many factors that “may” affect the generation of specific transgenic animals. Further, the Examiner questions the ability of the light-reporter system to be used in whole animals (Office action, pages 8-9). In regard to this last point the Examiner’s attention is directed to co-owned United States Patent 6,217,847, by Contag, et al., issued April 17, 2001, filed January 19, 1999 (this patent is a divisional of co-owned U.S. patent application Ser. No. 08/602,396, filed Feb. 16, 1996, now abandoned, which is continuation-in-part of co-owned U.S. patent application Ser. No. 08/270,631, filed Jul. 1, 1994, now U.S. Patent No. 5,650,135). A copy of this patent is being submitted with this paper. An overall summary of the Examiner’s rejection is stated on page 9, second full paragraph, of the Office action and recites the following:

Therefore, it is concluded that the specification fails to provide any guidance as to how an artisan would have dealt with the art recognized limitations of the method for making any and all transgenic animals and therefore, the creation of any and all non-human transgenic animals and their use in the recited methods would have necessitated undue experimentation on the part of an artisan.

The case law, however, does not support the Examiner’s position. Not every species encompassed by the claims, even in an unpredictable area like the chemical sciences, needs to be disclosed. (*In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976.) The notion that one of ordinary skill in the art must have reasonable

assurance of obtaining an active claimed product has been emphatically rejected (*Angstadt* at 219). So long as it is clear that some species render a composition operative, the inclusion of some possible inoperative species does not invalidate the claim under paragraph 1, of 35 U.S.C. §112. (*In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.) Further, even evidence of the need for some experimentation does not invalidate a claim on ground of undue experimentation, nor does it fulfill the PTO's burden of proof. (*In re Angstadt* at 504; *In re Morehouse*, 545 F.2d 162, 165, 192 USPQ 29,32, CCPA 1976.)

The law does not require an applicant to describe in his specification every conceivable embodiment of the invention. *SRI International v. Matsushita Elec. Corp. of America*, 775 F.2d 1107, 227 USPQ 577 (Fed. Cir. 1985). Further, the enablement requirement may be satisfied even though some experimentation is required. *Hybritech Inc. v. Monoclonal Antibodies*, 802 F.2d at 1367, 231 USPQ 81 (Fed. Cir. 1986).

However, in an effort to facilitate prosecution of this application, applicants have limited the current claims to transgenic mice. The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*Ex parte Forman*, 230 USPQ 546 (P.T.O. Bd. Pat. App. & Int., 1986). Specific references to some of the relevant teachings of the specification are provided in Section 1 above. Accordingly, the applicants submit that one of ordinary skill in the art could make and use the invention based on the disclosures in the patent coupled with information known in the art, without undue experimentation.

In view of the above arguments and amendments, the applicants submit that the specification provides sufficient working procedure for one skilled in the art to practice the invention as claimed without undue experimentation. The applicants submit that the claims are enabled. Applicants respectfully request that the rejection of the claims under 35 U.S.C 112, first paragraph, be withdrawn.

**3. Rejection of Claims 38, 40, 41, 43, 45, 49, and 65-68 under 35 U.S.C.
§112, Second Paragraph**

The Examiner has rejected claims 38, 40, 41, 43, 45, 49, and 65-68 under 35 U.S.C. §112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner has asserted the following specific deficiencies in the claims.

A. Claim 38

The Examiner asserts that recitation of the term “operable” is vague and indefinite. The Examiner has suggested use of the term “operably.” Applicants thank the Examiner for the Examiner’s careful attention to the language of the claims. Applicants have followed the suggestion of the Examiner and amended claim 38 to recite “operably.” The same language has been amended in claims 65 and 68.

B. Claim 40

The Examiner asserts that recitation of the phrase “selected control elements” is vague and indefinite. The phrase has been replaced by the phrase “control elements derived from stress-inducible genes” to provide correct antecedent basis relative to independent claim 38. The same language has been amended in claim 45.

C. Claim 45

The Examiner asserts that recitation of the phrase “a level expression” is vague and indefinite. The phrase has been replaced by the phrase “a level of expression,” wherein, the expression (i) is mediated by control elements derived from stress-inducible genes, and (ii) is in a non-human living animal.

In view of the above amendments, the teachings of the specification and the level of ordinary skill in the present art, the applicant submits that the boundaries of the claims are capable of being understood by one of ordinary skill in the art. Therefore, applicants respectfully requested that the rejection of the claims under 35 U.S.C. §112, second paragraph, be withdrawn.



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CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further communications in this application to:

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If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 325-7812.

Respectfully submitted,

Date: 21 June 2001

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5 **Marked-up claims corresponding to the amendments introduced in the accompanying paper:**

38. (Amended) A transgenic, [non-human animal] mouse comprising a panel of expression cassettes, said panel comprising

10 a first expression cassette comprising a first control element derived from a first stress-inducible gene, said control element [operable] operably linked to sequences encoding a first light generating polypeptide, and

15 a second expression cassette comprising a second control element derived from a second stress-inducible gene, said second control element [operable] operably linked to sequences encoding a second light generating polypeptide,

 wherein said expression cassettes have been introduced into said [animal] transgenic mouse or an ancestor of said [animal] transgenic mouse, at an embryonic stage.

20 40. (Amended) A method of determining the effect of an analyte on gene expression mediated by [selected] control elements derived from stress-inducible genes, wherein said expression is in a [non-human] living [animal] transgenic mouse, said method comprising

25 administering the analyte to a living transgenic [non-human animal] mouse of claim 38, wherein administering of said analyte is carried out under conditions that permit light generation mediated by said light generating polypeptide in the transgenic [animal] mouse,

30 determining the effect of the analyte on expression of the light generating polypeptide in a living [animal] transgenic mouse wherein said expression is mediated by at least one of the control elements.

41. (Amended) The method of claim 40, wherein said conditions that permit light generation mediated by the light generating polypeptide includes administering, to the [animal] transgenic mouse, at least one substrate for the light generating polypeptide.

5 43. (Amended) The method of claim 40, wherein the expression cassettes of said transgenic [animal] mouse comprise control elements derived from stress-inducible genes, and said analyte is screened for its affect on expression of stress-inducible genes.

10 45. (Amended) A noninvasive method for detecting a level of expression in response to an analyte, wherein said expression is (i) mediated by [selected] control elements derived from stress-inducible genes, and (ii) in a [non-human] living [animal] transgenic mouse, said method comprising

15 (a) administering the analyte to a living transgenic [non-human animal] mouse of claim 38, wherein administering of said analyte is carried out under conditions that permit light generation mediated by said light generating polypeptide,

 (b) placing the [animal] transgenic mouse within a detection field of a photo detector device,

 (c) maintaining the [animal] transgenic mouse in the detection field of the device, and

20 (d) during said maintaining, measuring photon emission from the [animal] transgenic mouse with the photo detector device to detect the level of expression of the light generating polypeptide in the living [animal] transgenic mouse wherein said expression is mediated by at least one of the control elements.

25 46. (Amended) The method of claim 45, further comprising, (e) repeating steps (b) through (d) at selected intervals, wherein said repeating is effective to detect changes in the level of the light emission in the [animal] transgenic mouse over time.

30 49. (Amended) A method of providing a transgenic, [non-human animal] mouse suitable for screening a selected analyte, comprising
 generating a transgenic [animal] mouse of claim 38, and
 providing said transgenic [animal] mouse or progeny thereof for use in screening a selected analyte.

5 65. (Amended) The transgenic [animal] mouse of claim 38, said panel further comprising

a third expression cassette comprising a control element derived from a third stress-inducible gene, said third control element [operable] operably linked to sequences encoding a third light generating polypeptide.

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66. (Amended) The transgenic [animal] mouse of claim 65, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.

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67. (Amended) The transgenic [animal] mouse of claim 65, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.

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68. (Amended) The transgenic [animal] mouse of claim 65, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different stress-inducible gene, said control element [operable] operably linked to sequences encoding a light generating polypeptide.